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Tamoxifen and angiogenesis

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Keywords

Angiogenesis, microvessel density, tamoxifen

Context

Angiogenesis, the development of a new blood supply from pre-existing vasculature, is essential for tumour growth beyond a few millimeters in diameter. Experimental evidence suggests that tamoxifen, a drug commonly used in breast cancer therapy, may possess anti-angiogenic properties as well as its antiestrogenic action. The aim of this study was to determine the effects of tamoxifen on breast tumour vascularity in patients who received adjuvant tamoxifen for 3-6 months prior to surgery.

Significant findings

A total of 75% of patients responded to tamoxifen, with tumour volume reduced up to 64%. Prior to treatment with tamoxifen there was no difference between microvessel counts (MVCs) in the responding and nonresponding tumours. MVCs were significantly reduced in tumours that responded to tamoxifen, and increased in the nonresponding cohort. Thus tamoxifen-responsive tumours show a significant reduction in tumour angiogenesis.

Comments

This is the first clinical study demonstrating a direct correlation of MVC with clinical response to tamoxifen. A related study (see Additional information) used a different approach to estimate angiogenesis, measuring vascular endothelial growth factor (VEGF), a circulating soluble marker of angiogenesis, as it has been argued that this is less subjective, more rapid and generally easier to perform. However, when the results are compared there is a discrepancy between the two methods:

Adams *et al*(see Additional information) found that treatment with tamoxifen resulted in an increase in circulating VEGF in breast cancer patients. It is important to note that surrogate markers of angiogenesis such as VEGF are produced in certain nonpathological conditions (e.g. during vascular remodelling of the endometrium and wound healing) and under certain physiological conditions, which may contribute to total systemic VEGF. The results of the present study are encouraging as they measure the MVC in the actual tumour. If the methodology can be standardised, their predictive value merits more detailed investigation in larger cohorts.

Methods

Immunohistochemistry, microvessel counts, ultrasound

Additional information

Adams J, Carder PJ, Downey S, Forbes MA, MacLennan K, Allgar V, Kaufman S, Hallam S, Bicknell R, Walker JJ, Cairnduff F, Selby PJ, Perren TJ, Lansdown M, Banks RE: **Vascular endothelial growth factor (VEGF) in breast cancer: comparison of plasma, serum and tissue VEGF and microvessel density and effects of tamoxifen.** *Cancer Res* 2000, **60**:2898-2905 (PubMed abstract).

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